DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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BETHESDA, MARYLAND 20014

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Peter F. Hall
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Dear Mr. Hall:

I am glad to hear that someone is still interested in an "ancient" paper of mine. That paper, as you know, is one of the first in a series related to the role of guanine nucleotides in hormone action on adenylate cyclase systems in membranes. As the first in a series, we naturally followed up many of the questions raised in this study. We know now, for example, that GTP contaminates both the membrane preparations and is a major contaminant in some commercial preparations of ATP. When these preparations are cleaned of contaminating GTP, hormone action does not occur without the addition of GTP. Our attempt to settle the question in the first paper was to incubate the membranes for a period of time prior to assay in order to "digest" any contaminating GTP in the membrane preparation. That experiment was not really conclusive; nonetheless, Fig. 5 gave us some feeling that GTP was important if not essential to the action of glucagon. Now we know that GTP and glucagon interact with separate protein molecules which are joined functionally to give a unit we termed R·N (R for receptor, N for nucleotide regulatory protein). The N unit is responsible for activating adenylate cyclase when liganed with GTP. The receptor seems to inhibit the ability of N to interact with GTP; binding of the hormone to R relieves this inhibition, allowing GTP to bind to N. Thus, N becomes activated by GTP and them combines (along with R) with adenylate cyclase to form the activated enzyme. This, in a grossly simplified form, is the status of the problem after nearly nine years of research. It goes on. Hope you and the others become interested in the problem. It still fascinates me.

Sincerely,

M. Rodbell

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